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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/142,628	Applicant(s) MYERS ET AL.	
	Examin r Michael Pak	Art Unit 1646	

-- The MAILING DATE of this communication app ars on th cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *18-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2, 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election of Group I in Paper No. 13 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 18-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 13.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1-17 and 25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S.

Patent No. 6,090,576. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1-17 and 25 of the present application encompass the same nucleic acid, vector, host cell, and the method of making protein as claims 1-11 of U.S. Patent No. 6,090,576. It would be obvious to one of ordinary skill in the art to use the nucleic acid, vector, host cell, and the method of making protein as claims 1-11 of U.S. Patent No. 6,090,576 to make or isolate the nucleic acid, vector, host cell, and the method of making protein of claims 1-17 and 25 of present application.

3. Claims 1-17 and 25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,440,701. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1-17 and 25 of the present application encompass the same nucleic acid, vector, host cell, and the method of making protein as claims 1-13 of U.S. Patent No. 6,440,701. It would be obvious to one of ordinary skill in the art to use the nucleic acid, vector, host cell, and the method of making protein as claims 1-13 of U.S. Patent No. 6,440,701 to make or isolate the nucleic acid, vector, host cell, and the method of making protein of claims 1-17 and 25 of present application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-17 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-17 and 25 encompass the terms "transferring receptor protein 1" and "transferring receptor protein 2" which is confusing because it is not clear what is the metes and bounds of the terms. It is not clear when a protein is structurally a "transferring receptor protein 1" versus a "transferring receptor protein 2" or another protein.

Claim 6 is indefinite for recitation of □stringent conditions□ which is a relative term and it is not clear whether the condition is high, moderate, or low stringency condition for hybridization. Furthermore, one skilled in the art use specific solutions for hybridization nucleic acid molecule. Claims 7-17 and 25 are dependent on claim 6 and encompass the term.

Claims 10 and 12 recite the term □having the characteristics□ which is ambiguous and confusing. It is not clear what characteristics are intended.

Claims 10 and 12 recite the term "pLEM3" and other vectors which is ambiguous and confusing. It is not clear what is the structure of the claimed vector and the metes and bounds of the term. It is not clear when a "pLem3" is different from "pLem25"

structurally.

5. Claims 1-17 and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid consisting of SEQ ID NO:1-6, does not reasonably provide the full scope of enablement for, A) nucleic acid encoding analog or equivalent of the tranferrin receptor protein, B) DNA with at least 90% sequence identity with SEQ ID NO:1-6. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims require that the nucleic acid encode a transferrin receptor, fragment or analog of the receptor. Analog is not defined in the specification and is deemed to embrace any protein differing in any way from the preferred embodiment coded for by SEQ ID NO: 1-6. The fragment or analog may be a functional transferrin receptor or it may be a protein or fragment having no particular function. Claims 1-17 encompass nucleic acid encoding variants of SEQ ID NO: 1-6 because of the recitation of an "analog" transferrin receptor protein which is not defined in the specification, and DNA which have the "characteristics of the disclosed plasmid" which is not defined in the specification. Analogs of claims 1-5, 9, 11, 13-17 encompass proteins with variant amino acid sequences as well as modified proteins which are cyclical or contain modified side chain groups. Claim 7 is directed to DNA which hybridizes to SEQ ID NO:1-6 and has 90% sequence identity with DNA encoding SEQ ID NO:7-12. However, a DNA which hybridizes does not have to encode a protein which is identical to the

protein of SEQ ID NO:7-12 and the DNA which has random 90% sequence identity may encode protein with substitutions anywhere along the protein. The state of the art is such that one skilled in the art cannot predict the outcome of changes to protein structure using the primary amino acid structure as the predictor (Bowie et al.(38), Science 1990). Thus, a substitution which causes improper folding will result in a non functional transferrin binding protein. For the same reasoning that variants are the source of unpredictability in determining ligand binding to transferrin receptor, the binding of antibodies to epitope depends on the tertiary structure of protein as determined by the primary amino acid sequence. The inability to predict the tertiary structure may lead to loss of epitope binding of the antibody or the inaccessibility of the epitope due to aberrant protein folding. The state of the art is such that epitope directed to the surface portion of the protein is likely to generate an antibody which binds the protein (Regenmortel(39), TIBS, 1986; page 37, middle column). No working example or guidance are provided to predict the tertiary structural changes of the variants which are functional as transferrin binding protein or as an epitope for the antibody. In view of the extent and the unpredictability of the experimentation required to practice the invention as claimed, one skilled in the art could not use the invention without undue experimentation.

6. Claims 1, 4, 5, and 9-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly

connected, to make and/or use the invention.

A deposit of the Moraxella bacterial strains is required to enable the invention of claims 1, 4, and 5. A deposit of plasmids in claims 10 and 12 are required to enable the invention of claims 9-14 . This determination has been made because the claimed strains or vectors have not been fully disclosed or the materials required to construct the claimed strains or vectors have not been shown to be publicly known and fully available. The specification does not teach how to make the disclosed strains or vectors, in a sufficient manner to practice the invention because one skilled in the art could not determine the exact materials necessary to construct the strains or the vectors. It would require undue experimentation to determine the exact materials necessary to construct the strains or vectors. Without a publicly available deposit of the above vectors or strains, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. A suitable deposit for patent purposes is required.

If a deposit has been made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating (a) that the deposit has been made under the terms of the Budapest Treaty; and (b) that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 C.F.R. □1.808.

If a deposit is not made under the terms of the Budapest Treaty, then the requirements may be satisfied by an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or by a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and establishing that the following criteria have been met: (a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto; (b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent; □ the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material; (d) a

viability statement in accordance with the provisions of 37 C.F.R. 1.807 is provided; and (e) the deposit will be replaced should it become necessary due to inviability, contamination, or loss of capability to function described in the manner in the specification.

In either case, the identifying information set forth in 37 C.F.R. 1.809(d) should be added to the specification if it is not already present. See 37 C.F.R. 1.803-1.809 for additional explanation of these requirements.

7. Claims 1-17, and 25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification generically describes as part of the invention isolated polynucleotides comprising the transferring receptor gene (see page 1, line 9). The specification also broadly describes their novel transferring receptor gene specifically by a novel reference polynucleotide sequence of SEQ ID NO:1-8, 48, 50, 51, 53, and 55. The specification broadly describes polynucleotides encoding the polypeptide of SEQ ID: 9-16, 49, 52, 54, and 56, to specifically include continuous or discontinuous regions encoding the polypeptide and may also contain additional coding and non-coding regions (see for example figure 7). First, it is evident from these pages of the specification that applicant is describing their novel transferring receptor gene specifically by a novel reference polynucleotide sequence (SEQ ID NO:1-8, 48, 50, 51, 53, and 55) and generically by and reference polynucleotide sequence encoding the novel polypeptide sequence (SEQ ID NO: 9-16, 49, 52, 54, and 56) and that such language is intended to encompass the "gene" and those coding or non-coding

sequences. Applicant also broadly describe the invention as embracing any substitution, insertion or deletion change of nucleotides throughout the entire stretch of nucleotides found in the reference sequence by use of language in which a specified number of nucleotides can be changed. As depending from these are the vectors, host cells and methods of producing the polypeptide. The claims encompass polynucleotide sequences *comprising* SEQ ID NO:1-8, 48, 50, 51, 53, and 55 sequences that have a recited degree of change as compared to a reference nucleic acid sequence comprising SEQ ID NO:1-8, 48, 50, 51, 53, and 55 sequences that hybridize to the full complement of SEQ ID NO: 1-8, 48, 50, 51, 53, and 55 and may or may not have transferring receptor function which correspond to sequences from other bacterial species, mutated sequences, allelic variants and *comprising* nucleic acids encoding SEQ ID NO:9-16, 49, 52, 54, and 56. None of these sequences meets the written description provision of 35 USC 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

The specification only discloses a polynucleotide sequence consisting of SEQ ID NO:1-8, 48, 50, 51, 53, and 55 which corresponds to the nucleic acid sequence encoding the *Moraxella catarrhal is* species of the protein which is a transferring receptor consisting of SEQ ID NO:9-16, 49, 52, 54, and 56. An isolated polynucleotide

consisting of a nucleotide sequence encoding SEQ ID NO:9-16, 49, 52, 54, and 56 is also described by way of the written description in view of the art established principle of wobble variants of triplet codons for particular bacterial amino acids as described in basic textbooks. Thus, an isolated polynucleotide sequence consisting of SEQ ID NO: 1 and an isolated polynucleotide consisting of a nucleotide sequence encoding SEQ ID NO:9-16, 49, 52, 54, and 56 meets the written description provision of 35 USC 112, first paragraph.

Applicants have not described nor disclosed the "operon" which encodes the transferring receptor gene. It is well known to one of skill in the art that a functional bacterial gene encompasses much more than a protein coding region. A bacterial gene is conventionally associated with positive and negative controlling elements such as promoters and repressors in a concordantly regulated transcription unit called an operon, without which, no protein is expressed. The specification fails to describe the functional gene *per se* (i.e., operon) and which applicants have intended to be encompassed by the comprising and encoding language of the instant claims as set forth *supra*. In a bacterial genome, the recitation of "comprising" SEQ ID NO:1-8, 48, 50, 51, 53, or comprising a nucleic acid encoding SEQ ID NO:9-16, 49, 52, 54, and 56, includes regulatory sequences which are essential to the operation and function of the structural gene in the operon. Moreover, the claims encompass and the specification contemplates and other open reading frames which are 3' and 5' to the polynucleotide sequence of SEQ ID NO:1-8, 48, 50, 51, 53, and similarly encoding the amino acid sequence of SEQ ID NO:9-16, 49, 52, 54, and 56, such 5' and 3' information inclusive of

the definition of an operon. These regulatory and other gene sequences of the operon that are not described, are essential to the function of the structural transferring receptor gene within the operon and are therefore essential elements. Such sequences fail to have an adequate written description in the instant specification. The specification does not provide written description support for any flanking nucleic acid sequences which are 5' or 3' of SEQ ID NO:1-8, 48, 50, 51, 53, and 55 or that which encodes SEQ ID NO: 9-16, 49, 52, 54, and 56. The specification does not provide any polynucleotide structure for a significant fragment or gene segment of the *Moraxella catarrhalis* genome, the polynucleotide sequence of the bacterial operon of which transferring receptor is a member or the gene in the operon as conventionally accompanied by the regulatory elements (i.e., regulatory regions such as promoters or repressors, termination codon), and which comprises SEQ ID NO:1-8, 48, 50, 51, 53, and 55. With the exception of an isolated polynucleotide consisting of SEQ ID NO:1-8, 48, 50, 51, 53, and 55 and an isolated polynucleotide consisting of a nucleotide sequence encoding SEQ ID NO:9-16, 49, 52, 54, and 56, the skilled artisan cannot envision all the contemplated nucleotide sequences by the detailed chemical structure of the claimed polynucleotides and therefore conception cannot be not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot

describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. Similarly, applicants have not disclosed any information which is 3' and 5' to the polynucleotide sequence of SEQ ID NO:1 and therefore clearly lacks written description for the broad class of polynucleotides comprising SEQ ID NO:1. Thus, the written description of the instant specification does not provide for "comprising" language. In the instant case the specification provides only written description for a polynucleotide consisting of SEQ ID NO:1-8, 48, 50, 51, 53, and 55 and a polynucleotide consisting of a nucleotide sequence encoding SEQ ID NO:9-16, 49, 52, 54, and 56.

Therefore, only an isolated polynucleotide consisting of SEQ ID NO:1-8, 48, 50, 51, 53, and 55 and an isolated polynucleotide consisting of a nucleotide sequence encoding SEQ ID NO:9-16, 49, 52, 54, and 56, but not the full breadth of the claim meets the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-5 and 9-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Gerlach et al. (S).

Gerlach et al. disclose the DNA, tfbA gene, which encodes the TfbA transferrin binding protein from Actinobacillus pleuropneumoniae (page 3256, Figure 2). Gerlach et al. disclose the method of cloning of the DNA encoding the TfbA transferrin binding protein by screening genomic DNA expression libraries with the antibodies to TfbA transferrin binding protein(page 3255, paragraph bridging the left and right columns; page 3257, paragraph bridging the left and right columns). Gerlach et al. disclose genomic DNA from various strains of A. Pleuropneumoniae bacteria probed with tfbA gene DNA under high stringency and medium stringency conditions on a Southern Blot (page 3259, left column and figure 6). Gerlach et al. teach that the bacteria actinobacillus pleuropneumonia causes percute to chronic porcine pleuropneumoniae(page 3253, left column, first paragraph). Gerlach et al. disclose the expression of vector comprising the Tbp in E.Coli transfected with the vector and isolation of the protein on an SDS-PAGE gel (page 3257, figure 3).

The rejected claims are directed to nucleic acid encoding an analog. Any transferrin receptor is an analog of the Moraxella receptor. The term "having the characteristics" is construed to mean encoding a receptor.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-17 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al.(R) in view of Gerlach et al.(S), Legrain et al.(T), Anderson et al.(U), and Gray-Owen et al.(V).

Yu et al. teach that Moraxella catarrhalis strain 4223 has two transferrin receptors, Tbp1 and Tbp2, and these proteins are similar to transferrin receptors found in other bacterial species such as N. meningitidis, Haemophilus influenza, and N. gonorrhoeae (page 434, second and third paragraph). Yu et al. teach the affinity

isolation of Tbp1 and Tbp2 from Moraxella catarrhalis 4223 strain and the SDS-PAGE isolation with a Western blot detected with the antibodies to Tbp1 and Tbp2 (page 440, figure 7; pages 443-444, "affinity isolation", "preparation of antisera", and "analytical methods"). Yu et al. disclose the method of generating antisera with purified Tbp1 or Tbp2 and the antibody use in the Western (page 440, figure 7; page 444, "preparation of antisera", and "Analytical methods"). Yu et al. teach that M. catarrahalis is associated with pneumonia, tracheitis, sinusitis and otitis media in children (page 433, introduction). Yu et al. do not teach the nucleic acid encoding Tbp1 or Tbp2 of Moraxella catarrhalis.

Gerlach et al. disclose the DNA, tfbA gene, which encodes the TfbA transferrin binding protein from Actinobacillus pleuropneumoniae (page 3256, Figure 2). Gerlach et al. disclose the method of cloning of the DNA encoding the TfbA transferrin binding protein by screening genomic DNA expression libraries with the antibodies to TfbA transferrin binding protein (page 3255, paragraph bridging the left and right columns; page 3257, paragraph bridging the left and right columns). Gerlach et al. disclose a Southern blot of genomic DNA from various strains of A. Pleuropneumoniae bacteria probed with tfbA gene DNA under high stringency and medium stringency conditions (page 3259, left column and figure 6). Gerlach et al. teach that the bacteria actinobacillus pleuropneumonia causes percute to chronic porcine pleuropneumoniae (page 3253, left column, first paragraph). Gerlach et al. teach that vaccination with one serotype or strain of bacteria does not protect against infection by bacteria from another serotype (page 3253, left column, second paragraph). Gerlach et al. teach that

the bacterial lipoproteins are important for metabolic functions for which an inhibitor may be used (page 3253, paragraph bridging the left and right columns). Gerlach et al. teach that several bacterial species such as Neisseria, Haemophilus influenza, Pasteurella haemolytica, and A. Pleuropneumoniae have transferrin binding protein which are used for binding transferrin of the natural host as an only source for iron (page 3253, right column, middle paragraph). Gerlach et al. teach that a tfbA gene DNA cloned previously does not bind tfbA gene of some strains of A. Pleuropneumoniae, and the different tfbA gene DNA can be cloned using this technique to elucidate the difference in structures between different strains of bacteria (page 3253, right column, middle paragraph; page 3260, left column, first paragraph). Gerlach et al. do not teach the nucleic acid encoding Tbp1 or Tbp2 of Moraxella catarrhalis.

Legrain et al. disclose the DNA, tbp1 and tbp2 genes, which encode the Tbp1 and Tbp2 transferrin binding protein from two strains of Neisseria meningitidis (page 73, abstract; pages 76-77, figures 2 and 3). Legrain et al. disclose the method of cloning of the DNA encoding the Tbp1 and Tbp2 transferrin binding protein by screening genomic DNA expression libraries with the antibodies to Tbp1 and Tbp2 transferrin binding protein(page 74, right column; page 75, figure 1). Legrain et al. disclose the construction of genomic libraries and the screening of the libraries using the DNA probe of tbp1 and tbp2 genes (page 75, figure 1). Legrain et al. teach that two clones of tfbA has been cloned by Gerlach et al. from Actinobacillus pleuropneumoniae and TfbA transferrin binding proteins have significant homology with Tbp1 transferrin binding protein of Legrain et al. (Page 76, figure 2; pages 76-77, column bridging the pages).

Legrain et al. teach that several bacterial species such as Neisseria gonorrhoeae and Haemophilus influenza have cross reactive epitope that bind antibodies (page 74, right column, top paragraph). Legrain et al. teach that transferrin binding proteins are used for binding transferrin for the source for iron which is an essential element for bacterial growth (page 73, left column, top paragraph). Legrain et al. do not teach the nucleic acid encoding Tbp1 or Tbp2 of Moraxella catarrhalis.

Anderson et al. disclose the DNA, tbpB gene, which encodes the Tbp2 transferrin binding protein from Neisseria gonorrhoeae (page 3162, abstract; page 3167, figure 7). Anderson et al. disclose the method of cloning of the DNA encoding the Tbp2 transferrin binding protein by screening chromosomal DNA libraries with the previously identified TbpA gene DNA probe; TbpA gene DNA encodes the Tbp1 transferrin binding protein (page 3164, right column, □Cloning of tbpB□). Anderson et al. disclose the expression of Tbp1 and Tbp2 proteins using expression vectors in a host cell and identifying and isolating the proteins on a Western Blot (page 3165, figure 2; pages 3165-3166, column bridging the pages and figure 3) Anderson et al. teach that Legrain et al. cloned DNAs which encode the Tbp1 and Tbp2 transferrin binding proteins from Neisseria meningitidis (page 3162, right column, last paragraph). Anderson et al. teach that DNAs encoding the Tbp1 and Tbp2 transferrin binding proteins cloned by Gerlach et al. from Actinobacillus pleuropneumoniae and Legrain et al. from Neisseria meningitidis have significant homology with Tbp1 and Tbp2 transferrin binding proteins of Anderson et al. (Page 3168, left column, second paragraph).

Anderson et al. do not teach the nucleic acid encoding Tbp1 or Tbp2 of Moraxella catarrhalis.

Gray-Owen et al. disclose the DNA, tbp1 and tbp2 genes, which encode the Tbp1 and Tbp2 transferrin binding protein from Haemophilus influenza (page 1201, abstract; pages 1202, right column; page 1203, figure 1; page 1204). Gray-Owen et al. disclose the method of cloning of the DNA encoding the Tbp1 and Tbp2 transferrin binding protein by screening genomic DNA expression libraries with the antibodies to Tbp1 and Tbp2 transferrin binding protein (pages 1202, right column). Gray-Owen et al. teach that DNA, tbp1 and tbp2 genes, from Haemophilus influenza have significant homology with DNA encoding Tbp1 and Tbp2 transferrin binding protein from Actinobacillus pleuropneumoniae, Neisseria gonorrhoeae, and Neisseria meningitidis(Page 1204; page 1207, right column). Gray-Owen et al. teach that Tbp proteins may be ideal vaccine candidates (page 1209, left column, last line). Gray-Owen et al. do not teach the nucleic acid encoding Tbp1 or Tbp2 of Moraxella catarrhalis.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to isolate the DNA encoding the Tbp1 or Tbp2 of Moraxella catarrhalis strain 4223 by using the antibody which binds Tbp1 or Tbp2 of Moraxella catarrhalis 4223 of Yu et al. as a probe to screen the genomic library of Moraxella catarrhalis by adapting the method of cloning of DNA encoding the Tbp1 or Tbp2 of Gerlach et al. One of ordinary skill in the art would have been motivated to clone the DNA encoding the Tbp1 or Tbp2 of Moraxella catarrhalis to confirm that they are related

to Tbp1 or Tbp2 of other bacterial species and to use the proteins for vaccines to treat M. catarrahalis associated pneumonia, tracheitis, sinusitis and otitis media in children. Yu et al., Gerlach et al., Legrain et al., Anderson et al., and Gray-Owen et al. provide evidence that Tbp1 or Tbp2 proteins are found in different species of bacteria and Gerlach et al., Legrain et al., Anderson et al., and Gray-Owen et al. provide evidence that DNA encoding Tbp1 or Tbp2 proteins are structurally related. The isolated DNA would encode the same Tbp1 and Tbp2 protein of Moraxella catarrhalis disclosed by Yu et al. and would inherently have the same amino acid sequences as SEQ ID NO: 9-16. It would have been obvious to one having ordinary skill in the art at the time the invention was made to screen the genomic library of other strains of Moraxella catarrhalis with the isolated Tbp DNAs using the method of Legrain et al. because Gerlach et al. teach the importance of elucidating differences in Tbp proteins in different strains of bacteria for vaccination. It would have been obvious to one having ordinary skill in the art at the time the invention was made to place the isolated Tbp DNAs in an expression vector and transform a host cell for the purpose of isolating the proteins recombinantly as taught by Anderson et al. because isolating pure protein could be used for vaccination. The specific vectors comprising the Tbp of claims 10 and 12 are obvious because one of ordinary skill in the art can place the isolated DNA in any vectors for the purpose of recombinant production of the protein in a host cell. Furthermore, claims 10 and 12 encompass vectors with similar properties as the disclosed plasmids because of the limitation of □having a characteristics of□ which is not defined in the specificaiton. The diagnostic kit of claim 25 comprises the nucleic

acid of claim 1 or 6 and thus encompasses the limitations of claim 1 or 6. It would have been obvious to one having ordinary skill in the art at the time the invention was made to screen other strains of Moraxella catarrhalis with the isolated Tbp DNAs (which is a diagnostic kit) using the method of Legrain et al. because Gerlach et al. teach the importance of elucidating differences in Tbp proteins in different strains of bacteria for vaccination.

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Shryvers(A) is cumulative reference with Yu et al.(R).

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Pak, whose telephone number is (703) 305-7038. The examiner can normally be reached on Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Michael D. Pak
Primary Patent Examiner
Art Unit 1646
22 August 2003